



UNITED STATES DEPARTMENT OF COMMERCE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/894,788	08/27/97	GIACOMONI	05725.0213

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FINNEGAN HENDERSON FARABOW  
GARRETT & DUNNER  
1300 I STREET NW  
WASHINGTON DC 20005

EXAMINER

CHANNAVAJJALA, L

ART UNIT

PAPER NUMBER

1502

DATE MAILED: 02/05/98

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

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# Office Action Summary

Application No.  
08/894,788

Applicant(s)  
Paolo Giacomoni

Examiner  
Lakshmi Channavajjala

Group Art Unit  
1502



- ☐ Responsive to communication(s) filed on \_\_\_\_\_
- ☐ This action is **FINAL**.
- ☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

## Disposition of Claim

- ☒ Claim(s) 31-64 \_\_\_\_\_ is/are pending in the application.
- Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration
- ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- ☒ Claim(s) 31-64 \_\_\_\_\_ is/are rejected.
- ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- ☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.

## Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- ☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

- ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☒ All ☐ Some\* ☐ None of the CERTIFIED copies of the priority documents have been
- ☒ received.
- ☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

- ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

- ☒ Notice of References Cited, PTO-892
- ☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 3
- ☐ Interview Summary, PTO-413
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

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***Claim Rejections - 35 USC § 112***

1. Claims 39 and 55 recites the limitation "2-(5,6,7,8-tetrahydro-5,5,5,8,8,-tetramethyl-2-naphthyl)-6-benzothiophenecarboxylic acid, 6-[3-(1-adamantyl)-4-methoxyphenyl]-2-naphthanoic acid or 3-Pyridinecarboxylic acid" in lines 2-4 of the claims. There is insufficient antecedent basis for this limitation in the claim.

***Claim Rejections - 35 USC § 103***

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 31-34, 43-45 and 59-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Teale in view of Williamson et al. The invention of Teale relates to a pharmaceutical composition comprising a inhibitor of nitric oxide synthase and an anti-inflammatory agent for the treatment of systemic inflammatory response syndrome. The anti-inflammatory agents include corticosteroids (see page 3, line 2- 7) and nitric oxide synthase inhibitors such as aminoarginine (page 3, lines 12-15), in a pharmaceutically acceptable carrier (page 3, lines 17-18). The concentration of the nitric oxide synthase inhibitor used by Teale is within the range of the concentrations claimed by the applicant (page 4, line 41). However, Teale does not teach the incorporation of cosmetic or pharmaceutical compounds causing cutaneous irritating effect.

Williamson et al teaches a method of inhibiting nitric oxide formation in mammals by the administration of methyl-, dimethyl or amino substituted guanidines (column 1, 22-27). Among the various chronic and acute inflammatory conditions, Williamson et al teaches dermatitis, drug

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reactions, sunburn, insect bites, burns (thermal, chemical and electrical) (column 3, lines 38-45). Williamson et al does not teach the nitric oxide synthase inhibitors claimed in the present invention. However, it would have been obvious to one of ordinary skill in the art to incorporate nitric oxidase synthase inhibitor, amino arginine in the teachings of Williamson et al, since the skin disorders which Williamson et al teaches does involve cause cutaneous irritation. Such a combination would allow one to highly diminish the skin irritating effects of cosmetic or pharmaceutical compositions by efficiently inhibiting the production of nitric oxide by nitric oxide synthase.

2. Claims 35 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Teale in view of Wilhelm et al and Williamson et al.

Wilhelm et al studied the surfactant-induced irritation skin reactions by exposing volunteers to surfactants such as sodium lauryl sulfate, dodecyl trimethyl ammonium bromide and potassium soaps. Their studies showed that the chronic irritation in their model represents the clinical situation of irritant contact dermatitis with pronounced skin dryness (see abstract). Wilhelm et al, however, did not teach a method of inhibiting the surfactant induced skin irritation.

The teachings of Teale and Williamson et al, discussed above, have been relied upon for the same. The teachings of Teale and Williamson et al does not show the skin irritation caused by surfactants. However, it would have been obvious for a skilled artisan to include nitric oxide synthase inhibitors in a pharmaceutical or cosmetic composition containing surfactants, since the surfactants may lead to the production of nitric oxide by stimulating nitric oxidase (as taught by Williamson et al) thus leading to skin irritation and eventually dermatitis.

3. Claims 36-39, 47, 52-55, 63 and 64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et al in view of Williamson et al.

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Yu et al teaches a preventive as well as therapeutic treatment to alleviate the cosmetic conditions and symptoms of dermatologic disorders (page 2, lines 25-30; page 11, lines 11-13) by administration of alpha hydroxy acids, alpha ketoacids and related compounds (page 1, lines 1-3 and page 10, lines 29-36). Yu et al also teaches incorporation of salicylic acid (page 2, lines 1-2), and a number of other cosmetic and pharmaceutical agents (page 10, lines 6-24) in the therapeutic treatment. In addition, Yu et al also teaches that these alphydroxy acids, alpha keto acids and related compounds present in the cosmetic or therapeutic compositions may irritate the human skin or repeated topical applications due to the lower pH of the formulation. However, the teachings of Yu et al does not suggest a method of inhibiting the skin irritation caused by these compounds.

The teachings of Williamson et al, discussed above, suggest the inhibition of nitric oxide synthase in a variety skin disorders, which involve skin irritation. Although Williamson et al does not particularly teach the inhibition of cutaneous irritation caused by the compounds claimed in the present invention, it would have been obvious for one of ordinary skill in the art to include nitric oxide synthase inhibitors in any pharmaceutical or cosmetic composition, in which the cosmetic or pharmaceutical compounds might possibly exert a cutaneous irritating effect, and thus reduce the adverse reactions caused by these compounds.

4. Claims 45, 46, 61 and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Teale in view of Ahluwalia et al.

The teachings of Teale have been discussed above. Teale teaches only amino arginine for inhibiting nitric oxide synthase. Ahluwalia et al teaches a number of nitric oxide synthase inhibitors used for skin application to reduce the hair growth (see column 1, lines 50-61). It would have been obvious for one of ordinary skill in the art to include all the nitric oxidase synthase inhibitors taught by Ahluwalia et al in the teachings of Teale to effectively reduce the skin irritating characteristics of the various cosmetic and pharmaceutical compounds.

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5. Claims 40, 41, 56 and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pillai et al in view of Teale. The teachings of Teale and Williamson et al have been discussed earlier. However, their teachings lack Vitamin D and its derivatives in the cosmetic or pharmaceutical compositions. Pillai et al teaches compositions containing Vitamin D derivative (1,25-hydroxy-D3) for treating skin, hair and nails (column 1, lines 55-63). Pillai et al teaches that exogenously applied 1,25-hydroxy-D3 is converted to 1,25-dihydroxy-D3 and the latter has toxic side effects (column 3, lines 1-30). Pillai et al does not teach nitric oxide synthase inhibitors to reduce the side effects of 1,25-dihydroxy-D3. However, it would have been obvious for one of ordinary skill in the art to incorporate nitric oxide synthase inhibitor suggested by Teale in the pharmaceutical composition of Pillai et al to inhibit the side effects of these skin treating vitamins.

6. Claims 42 and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Philippe et al in view of Teale and Williamson et al. Philippe et al teaches the use of lipophilic quarternary ammonium salicylates in cosmetics and in dermaopharmacy (column 1, lines 18-33). The preferred compounds include 5-octanoylsalicylate and 5-dodecanoylsalicylate (column 4, lines 10-35) and can be used for a variety of pharmaceutical and cosmetic conditions (columns 5 and 6). Although Philippe et al does aim at reduced skin irritancy of the above compounds (column 2, lines 32-36) and inclusion of anti-inflammatory compounds in the composition (column 5, lines 4-10), their teachings does not include nitric oxide synthase inhibitors which are anti-inflammatory as well as reduce skin irritation. The teachings of Teale and Williamson et al, discussed above, were relied upon for the same. Although both Teale and Williamson et al teach nitric oxide synthase inhibitors, neither of them teach salicylic acid derivatives for treating skin conditions in their compositions. However, it would have been obvious for one of ordinary skill in the art to incorporate nitric oxide synthase inhibitors in the composition of Philippe et al and successfully inhibit the skin irritancy caused by the lipophilic quarternary ammonium salicylates.

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*Correspondence*

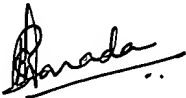
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lakshmi S. Channavajjala whose telephone number is (703) 308-2438. The examiner can normally be reached Monday through Friday from 8:00am to 4:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page, can be reached on (703) 308-2927. The fax number for this Group is (703) 305-5408.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. § 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [thurman.page@uspto.gov].

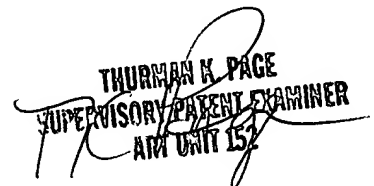
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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703-305-2351)



Lakshmi S. Channavajjala

01/26/98



THURMAN K. PAGE  
SUPERVISORY PATENT EXAMINER  
ART UNIT 152